

Figure 1

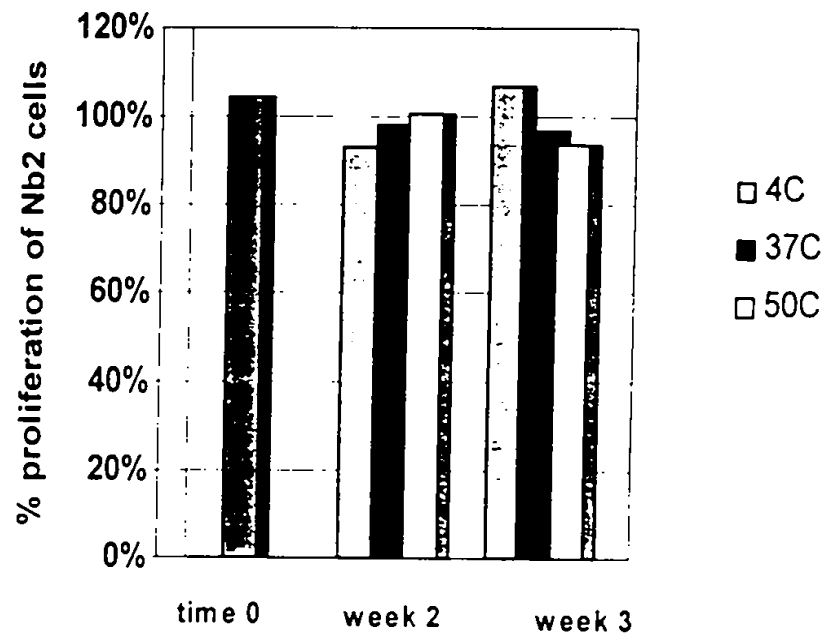


Figure 2

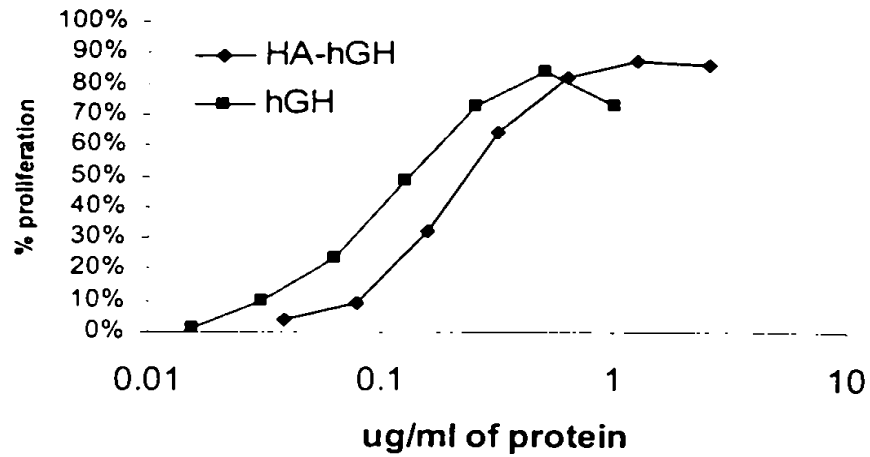


Figure 3A

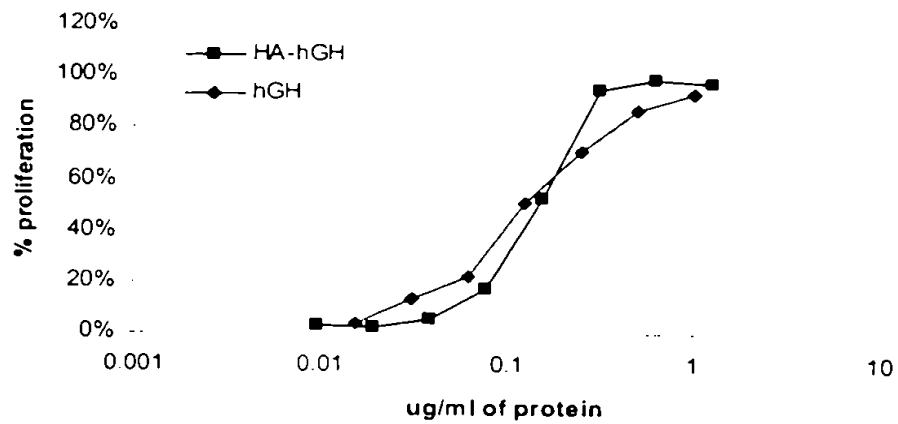


Figure 3B

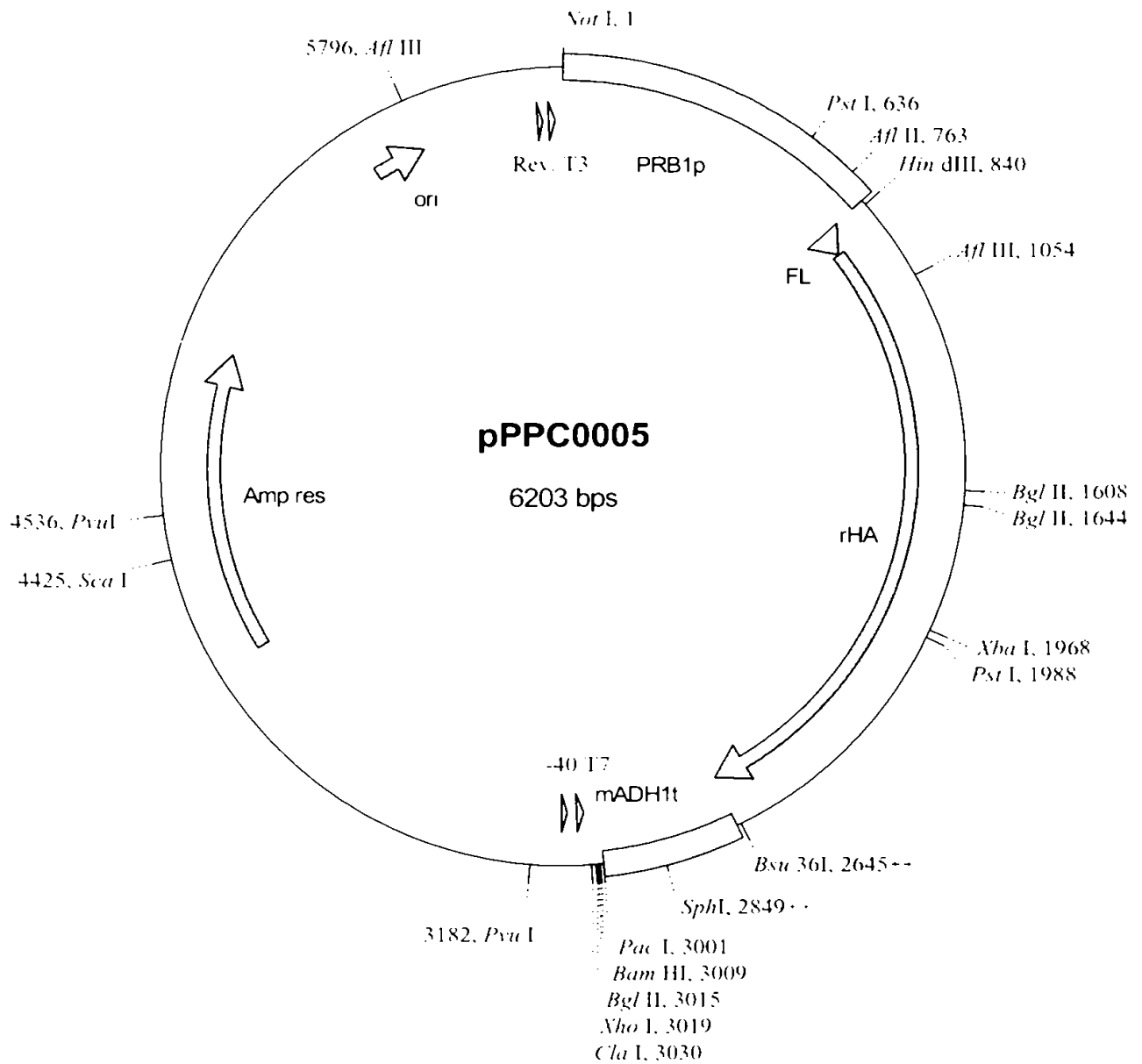


Figure 4

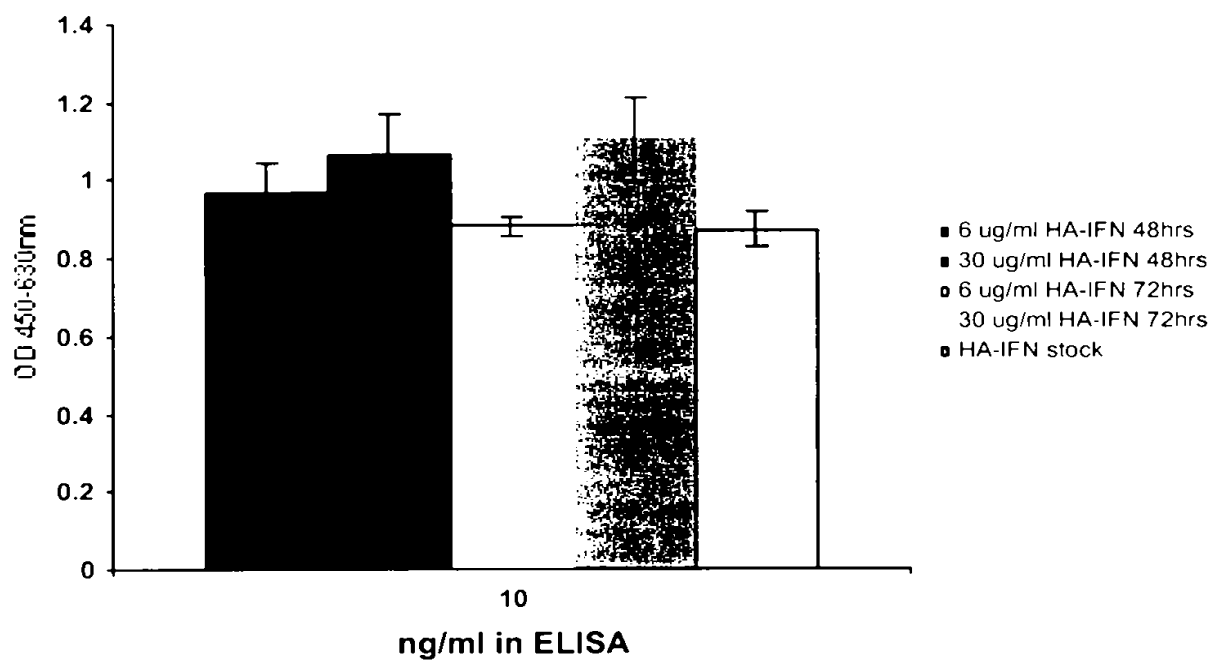


Figure 5

Figure 6

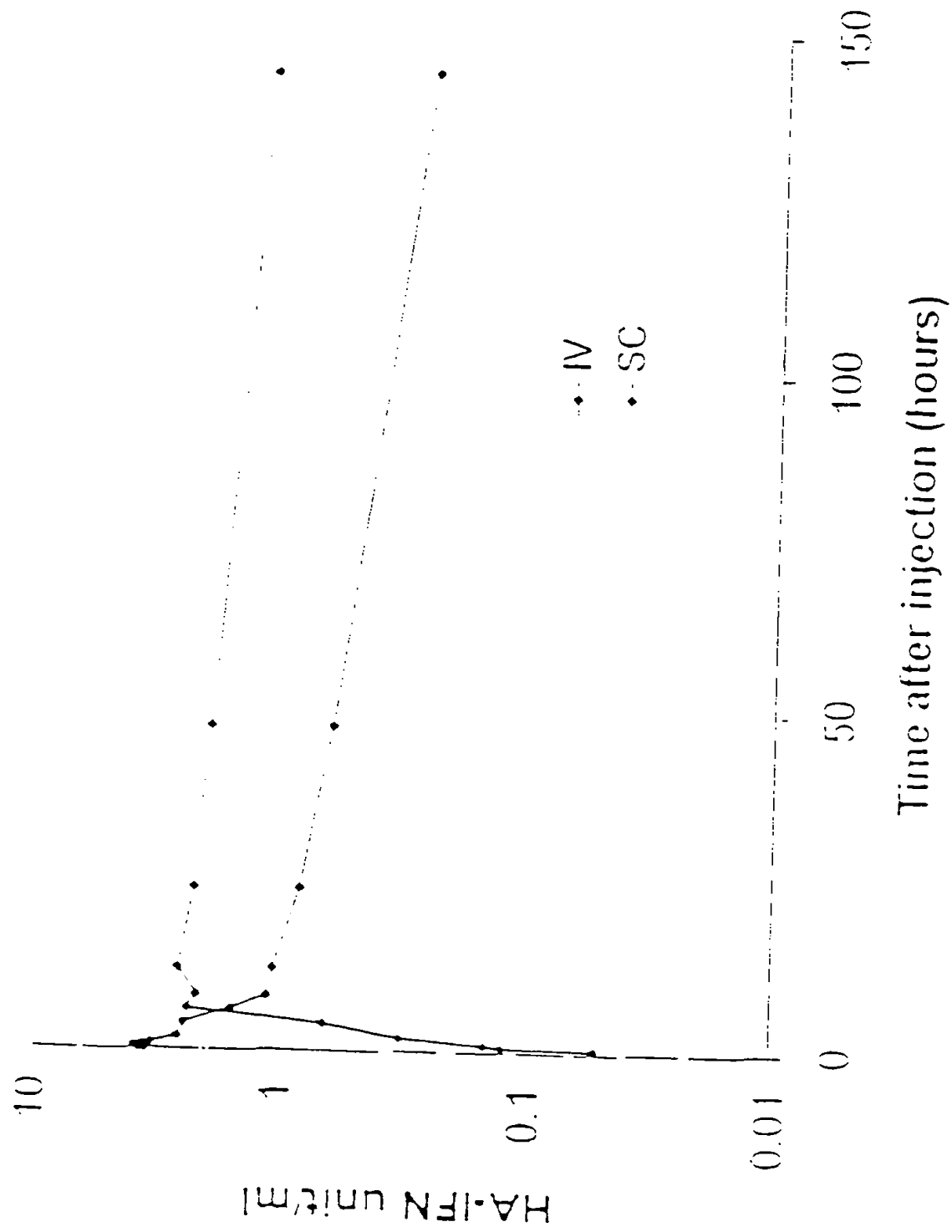
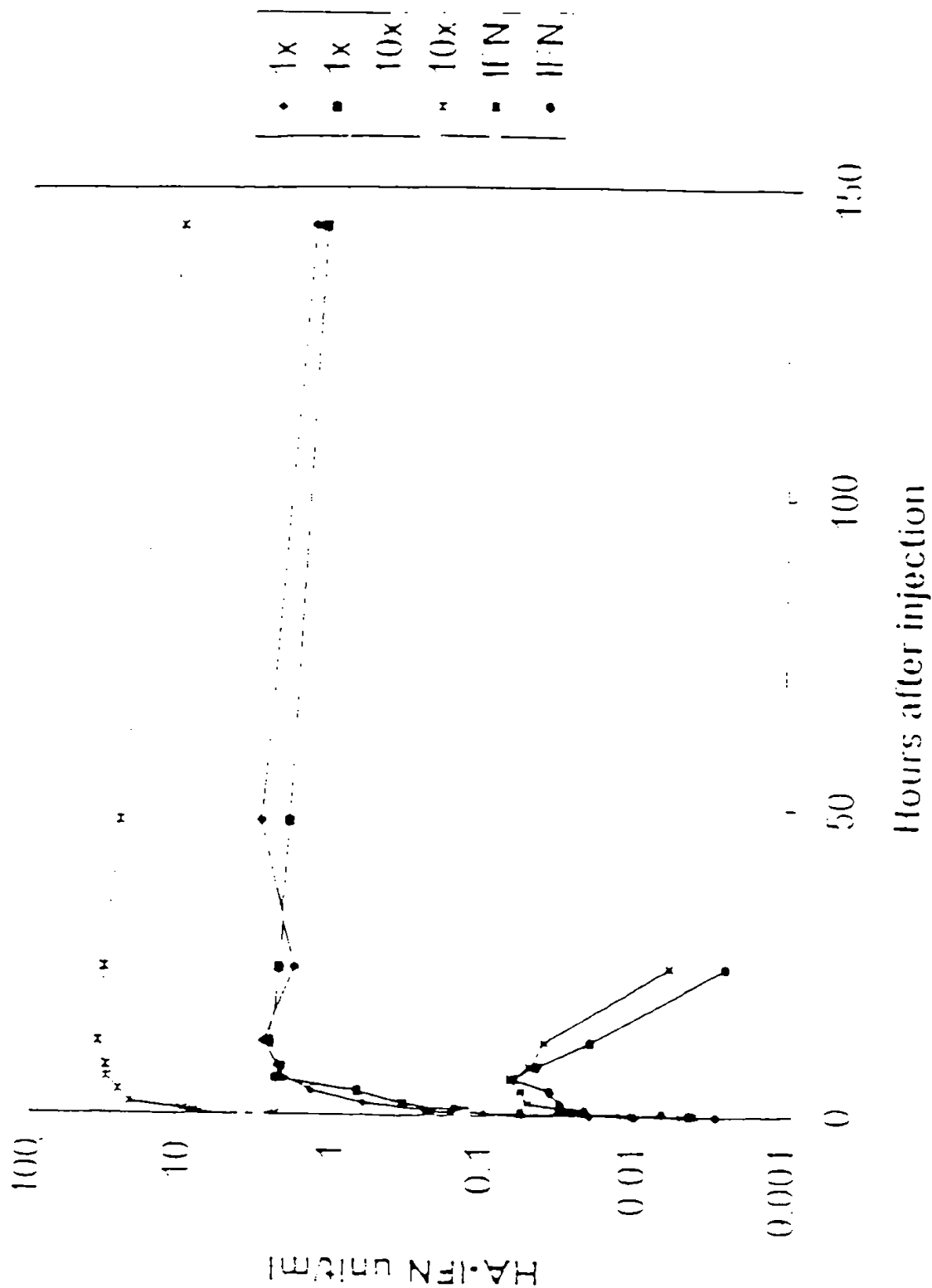


Figure 7



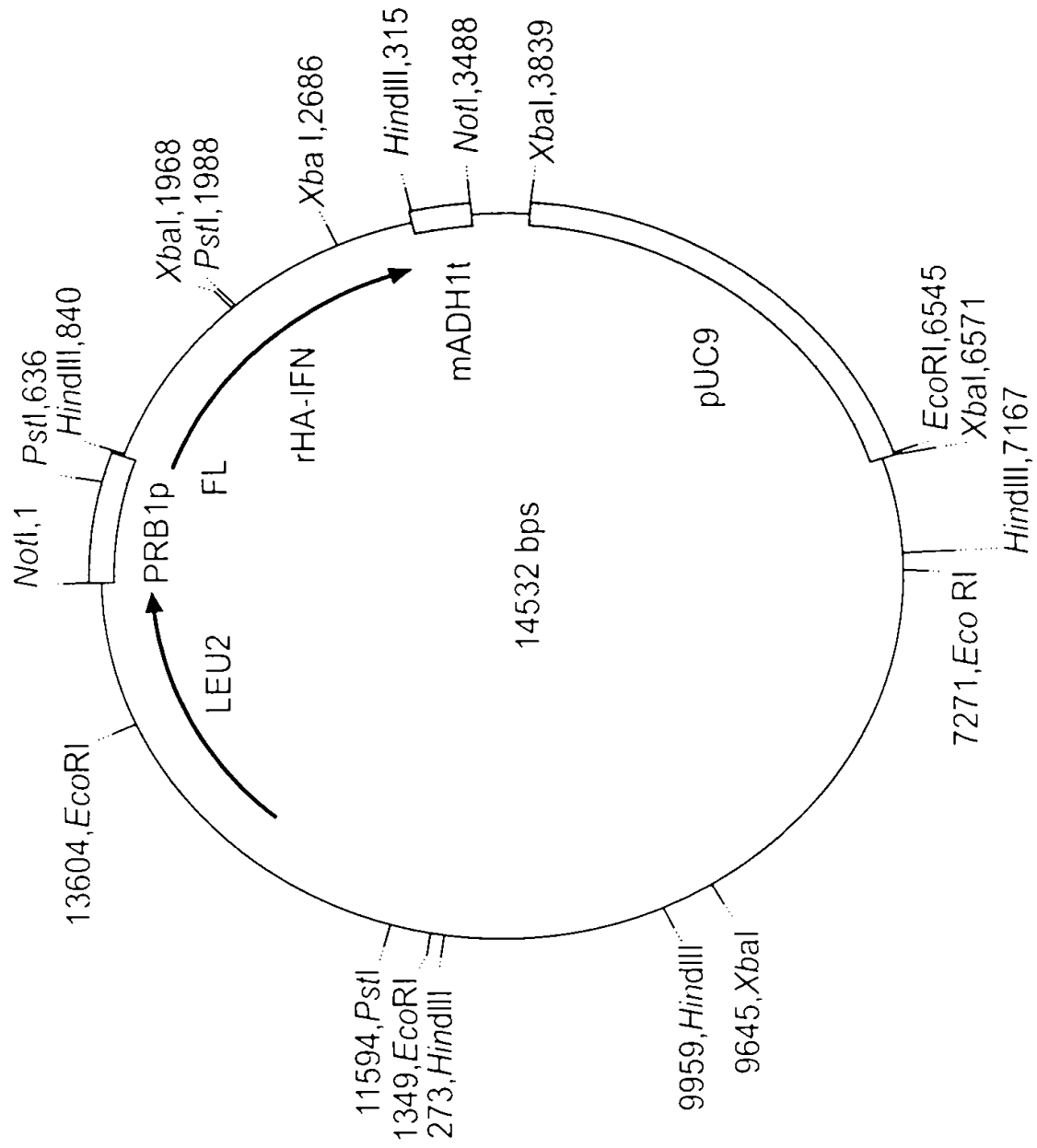


FIG. 8

Figure 9

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1    DAHKSEVAHR FKDLGEENFK ALVLIAFAQY LQCCPFEDHV KLVNEVTEFA
      HHHHH HHH      HHH HHHHHHHHHHH      HHHHH HHHHHHHHHHH

      I                      II                      III
51   KTCVADESAE NCDKSLHTLF GDKLCTVATL RETYGEMADC CAKOEPERNE
      HHHHH      HHHHH HHHHH      HHHH H      HHHH

101  CFLQHKDDNP NLPRLVRPEV DVMCTAFHDN EETFLKKYLY EIARRHPYFY
      HHHH      H      HHHHHHHHH      HHHHHHHHH HHHHH

      IV
151  APELLFFAKR YKAAFTECO AADKAACLLP KLDELRLDEGK ASSAKQRLKC
      HHHHHHHHHH HHHHHHHHH      HHHHH HHHHHHHHHH HHHHHHHHHH

      V
201  ASLQKFGERA FKAWAVARLS QRFPKAEFAE VSKLVTDLTK VHTECCHGDL
      HHHHH      HH HHHHHHHHHH HH      HHH HHHHHHHHHH HHHHHH      HH

      VI                      VII
251  LECADDRADL AKYICENODS ISSKLECCE KPLLEKSHCI AEVENDEMPA
      HHHHHHHHHH HHHHH      HHHHH      HHHHHHHH H

301  DLPSLAADFV ESKDVCKNYA EAKDVFLGMF LYEYARRHPD YSVVLLRLA
      HHHH      HHHHHH      HHHHHH      HHHHHH      HHHHHHHH

      VIII
351  KTYETTLKCK CAAADPHECY AKVFDEFKPL VEEPQNLIKQ NCELFEQLGE
      HHHHHHHHHH      HH      H      HHHHH HHHHHHHHHH HHHHHH

      IX
401  YKEQNALLVR YTKKVPQVST PTLVEVSRNL GKVGSKCCKKH PEAKRMPCAE
      HHHHHHHHHH HHHH      H      HHHHHHHHHH      HHH      HHHHHHHH

      X                      XI
451  DYLSVVLNQL CVLHEKTPVS DRVTKCOTES LVNRRPPCFSA LEVDETYVPK
      HHHHHHHHHH HHHHH      HHHHHHHHH      HHHHHHHH

501  EFNAETFTFH ADICTLSEKE RQIKKQTALV ELVKKHKPKAT KEQLKAVMDD
      HHH      HHH HHHHHHHHHH HHH      HHHHHHHH

      XII
551  FAAFVEKCKK ADDKETCPAE ECKKLVAASQ AALGL
      HHHHHHHH      HHHH HHHHHHHHHH HH
  
```

Loop

I Val154-Asn161
 II Thr176-Asp189
 III Ala190-Glu190
 IV Gln170-Ala176
 V His247-Glu252
 VI Glu166-Glu277

Loop

VII Glu280-His288
 VIII Ala362-Glu368
 IX Lys439-Pro447
 X Val460-Lys475
 XI Thr478-Pro486
 XII Lys560-Thr566

Figure 10

a. Randomisation of Loop IV.

IV
 151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

IV
 151 APELLFFAKR YKAAFTECCX XXXXXXXXCLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

X represents the mutation of the natural amino acid to any other amino acid. One, more or all of the amino acids can be changed in this manner. This figure indicates all the residues have been changed.

b. Insertion (or replacement) of Randomised sequence into Loop IV.

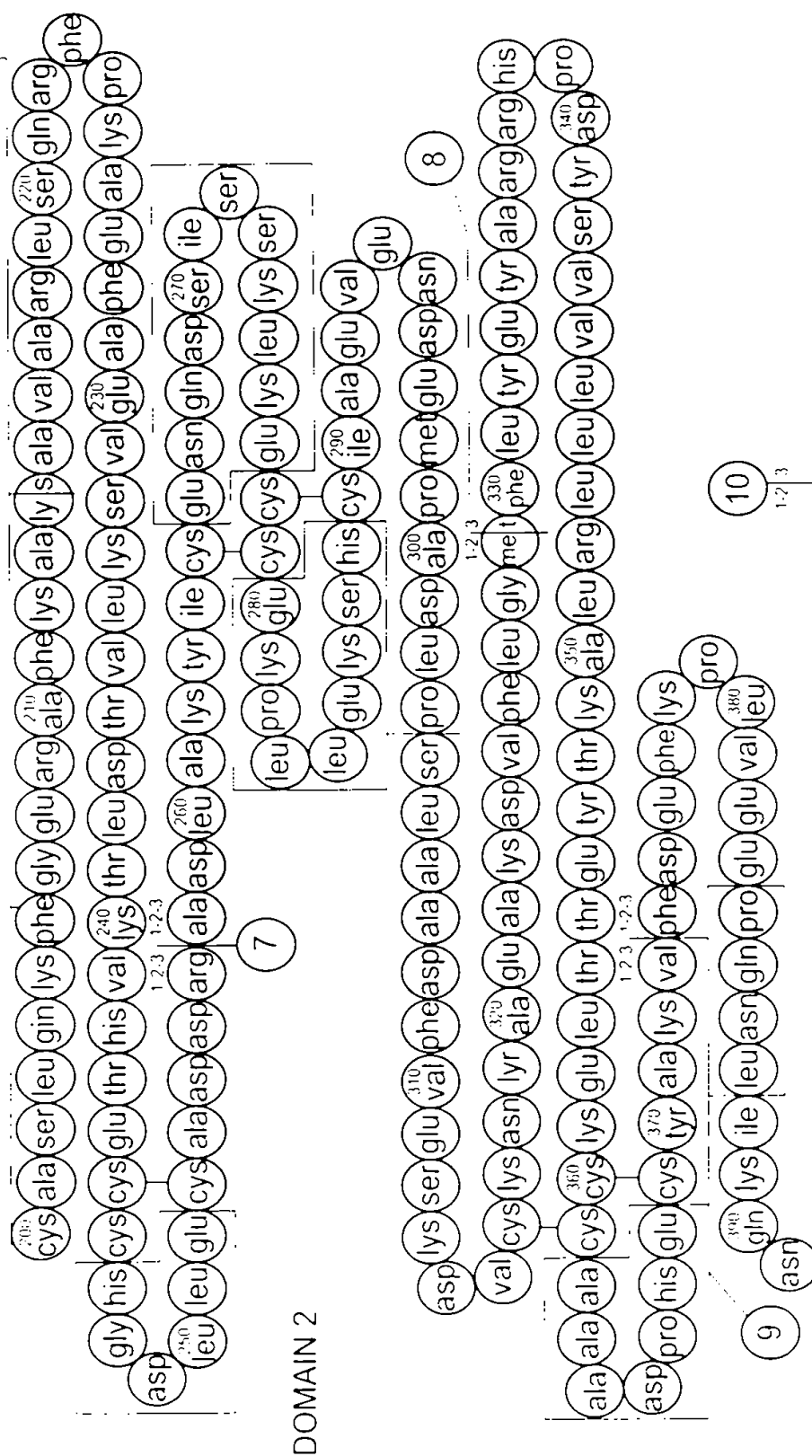
(X)_n



IV
 151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

The insertion can be at any point on the loop and a length where n would typically be 6, 9, 12, 20 or 25.

FROM FIG. 11A



TO FIG. 11C

TO FIG. 11C

FIG. 11B

FROM FIG. 11B

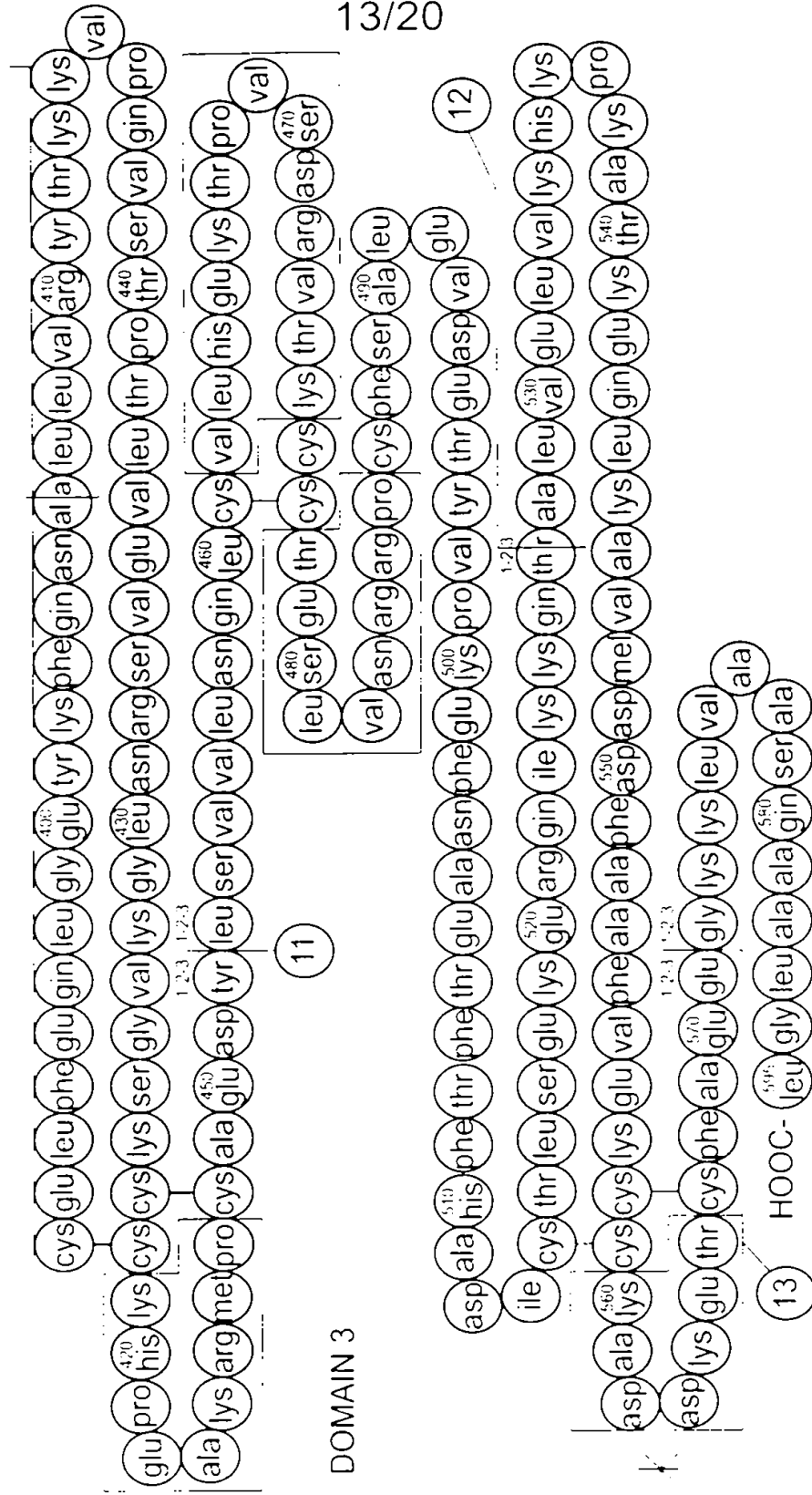


FIG. 11C

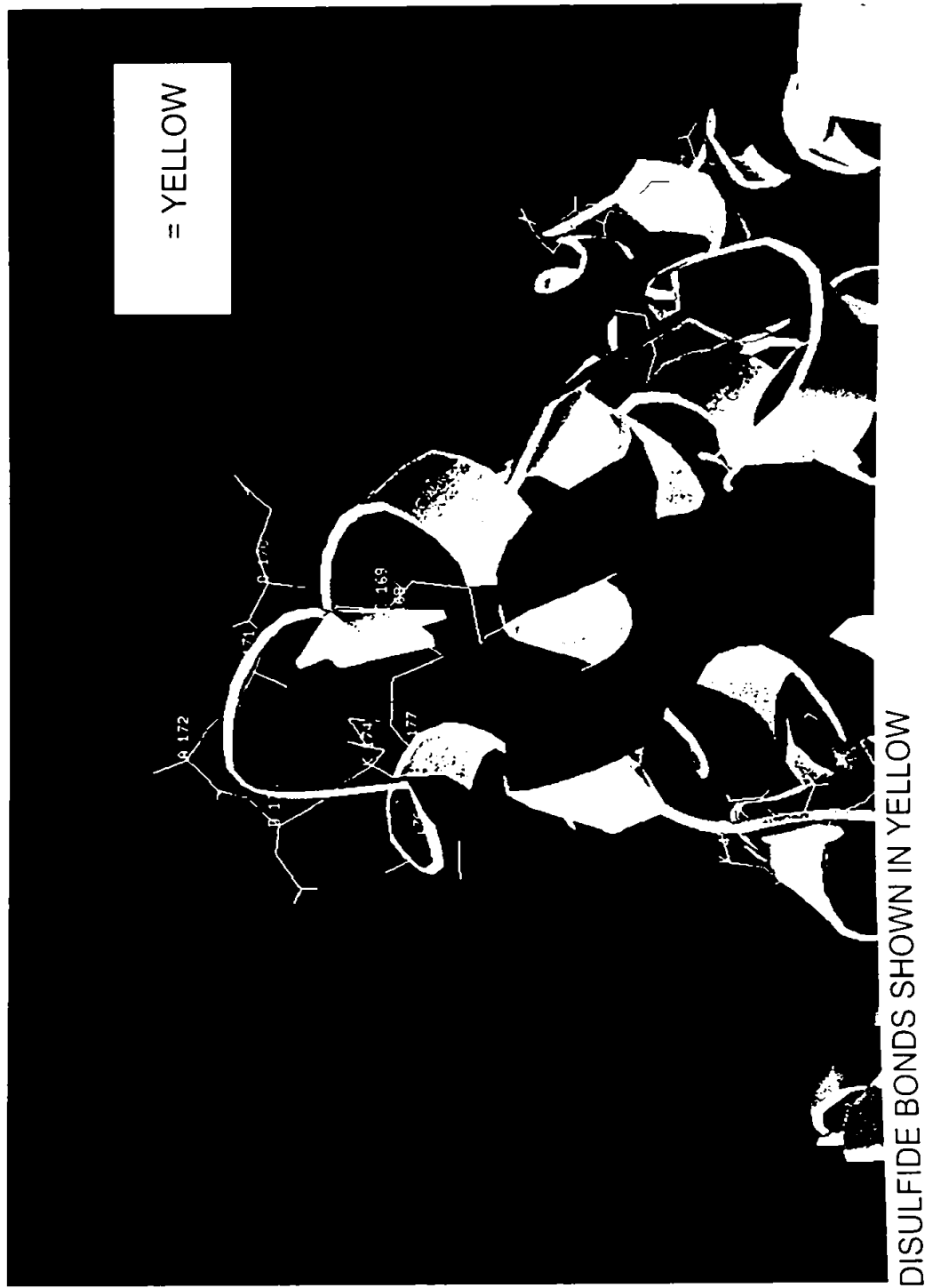


FIG. 12:
LOOP IV GLU170-A176

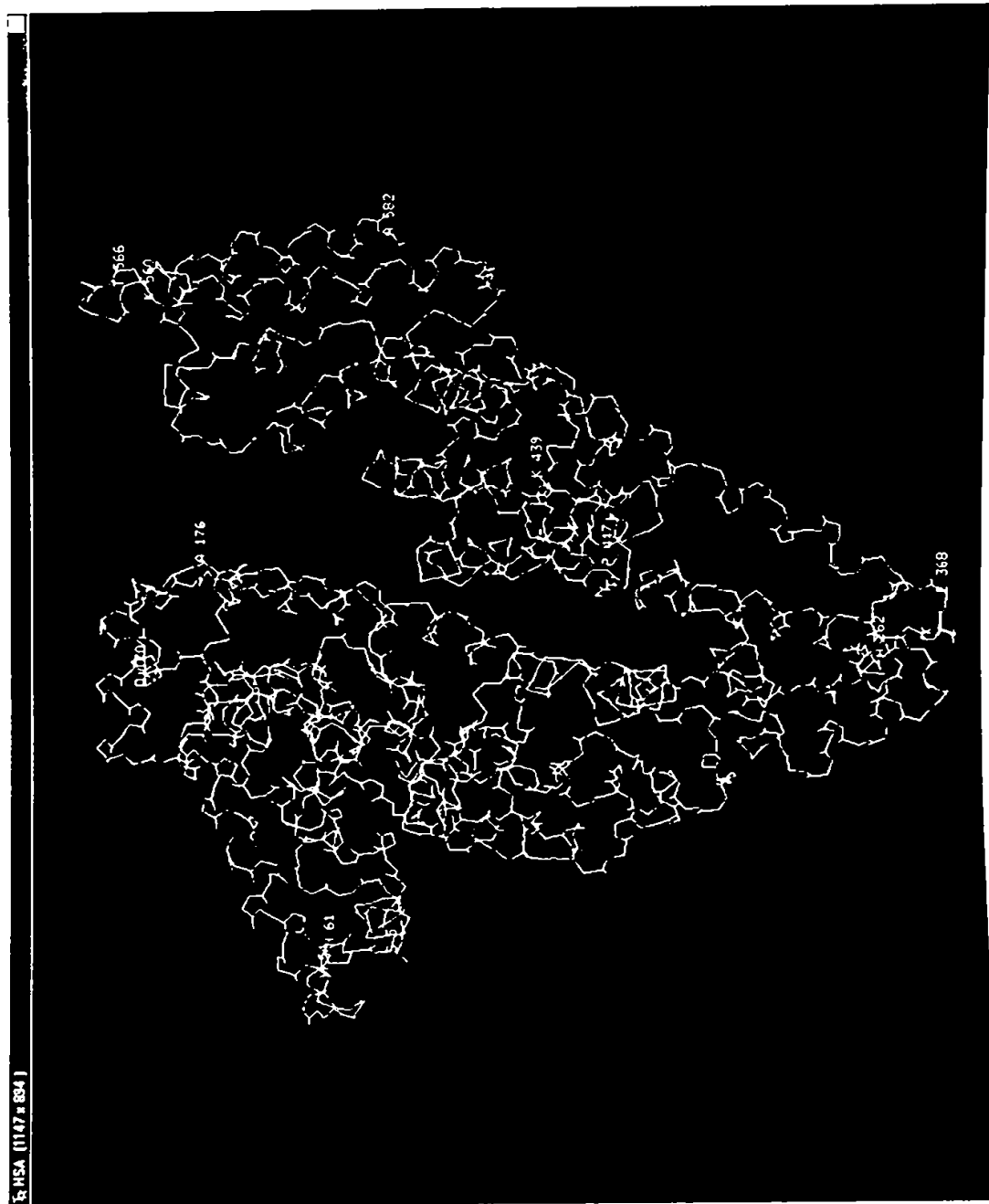


FIG. 13
TERTIARY STRUCTURE OF HA

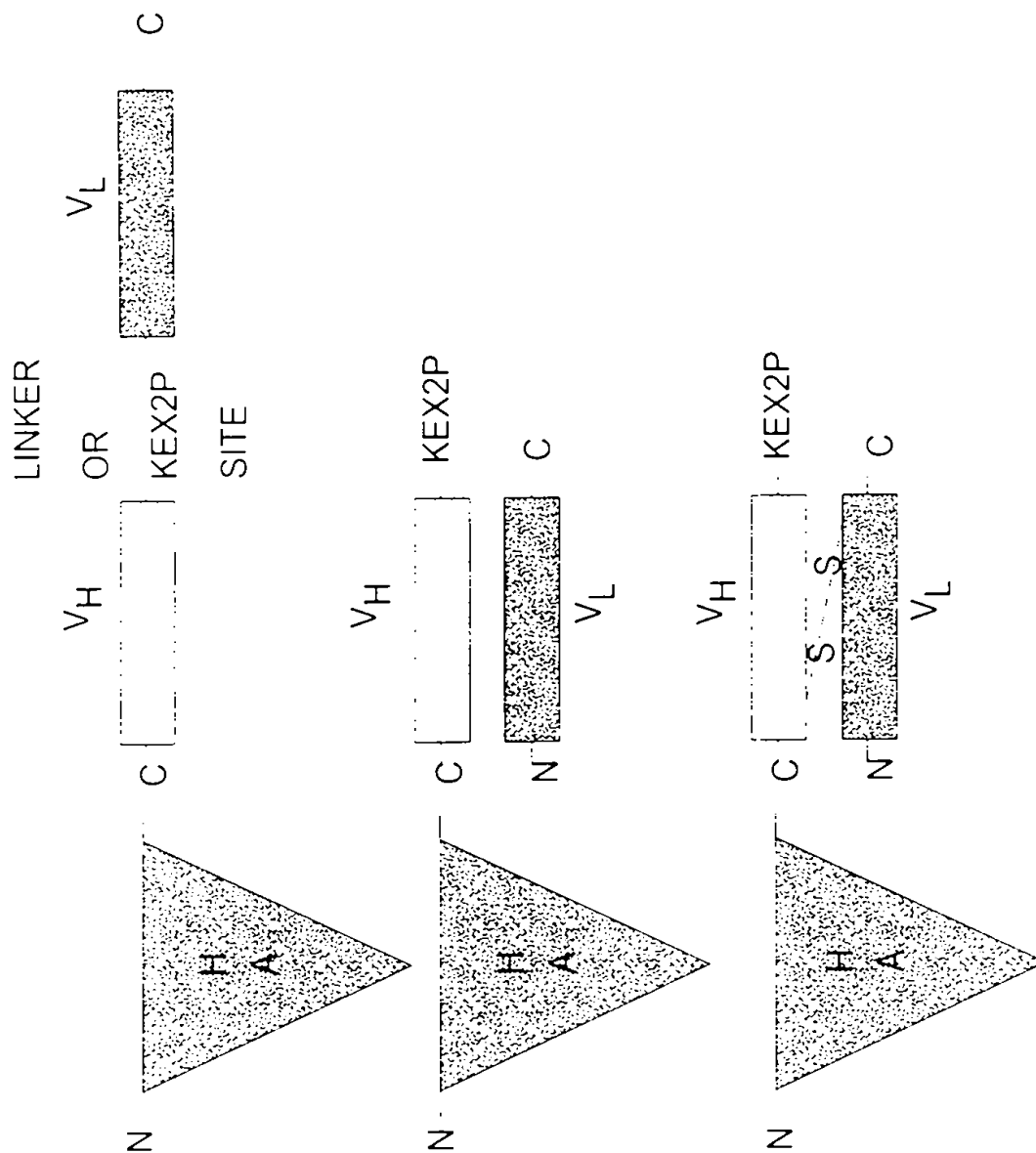


FIG. 14

Figure 15A

481 TAT AAA GGT GGT TTT AAA GAA TGT TAT CAA GCT GGT GAT AAA GCT GGC TGC CTG TTG CCA 540
 161 Y E A A F T E C C Q A A A D K A A C L L P 180

541 AAG CTC GAT GAA CTT GCG GAT GAA GAG AAG GCT TGG TCT GCG AAA CAG AGA CTC AAA TGT 600
 181 F I D E L E R D E G E A S S A K Q R L K C 200

601 TCG AAT CTC GAA AAA TTT GGA GAA AAG GCT TTC AAA GCA TGG GCA GTG GCT CGC CTG AGC 660
 201 A S L Q K F G E K A E K A F K A W A V A R L S 220

661 CAG AGA TTT GCG AAA GCT GAG TTT GGA GAA GGT TGC AAG TTA GTG ACA GAT CTT ACC AAA 720
 221 Q R F E F A E E A E V S K L V T D L T K 240

721 GTC CAC ACG GAA TGT TCG GAT GAA GAT CTG CTT GAA TGT GCT GAT GAC AGG GCG GAC CTT 780
 241 V H T E C C C E G E D L L E C A D D R A D L 260

781 TCG AAG TAT ATT TGT GAA AAA CAG GAT TCG ATC TCG ACT AAA CTG AAG GAA TGC TGT GAA 840
 261 A E Y I C E H D D G I S S K L K E C C E 280

841 AAA GCT CTG TTG GAA AAA TCG CAC TGC ATT GTC GAA GTG GAA AAT GAT GAG ATG CCT GCT 900
 281 K F L L E R S H C I A E V E H D E M P A 300

901 GAC TTG GCT TCA TTA GCT GCT GAT TTT GTT GAA ACT AAG GAT GTT TGC AAA AAC TAT GCT 960
 301 D L P S L A A D F V E S K D V C K N Y A 320

Figure 15B

461 GAG GCA AAG GAT GTC TTC CTG GGC AAG TTT TTG TAT GAA TAT GCA AGA AGG CAT CCT GAT 1020
 471 E A K D V F L G M F L Y E Y A R R H P D 340

1001 TAC TGT GGT TEG CTG CTG CTG AAG GTT TAC AAG ACA TAT GAA AGC ACT CTA GAG AAG TGC 1980
 1011 Y A Y V L L L L R L A K T Y E T T L E K C 360

1091 TGT GGT GGT GCA GAT GGT GAT GAA TAT GGC AAA GTG TTG GAT GAA TTT AAA CCT CTT 1140
 1101 C A A A D I E L Y A K V F D E F K P L 380

1181 GTG GAA GAG GGT GAG AAA TTA AGT AAA GCA AAC TGT GAG GAG CTT GGA GAG 1200
 1191 V E E F Q D I I K V H C E L F E Q L G E 400

1281 GAC AAA TTC GAT AAG GTC GTC TTA GTC GGT TAC AAG AAG AAA GTA CCC CAA GTG TCA ACT 1260
 1291 E E E L A L L E V R Y T K K V P Q V S T 420

1361 GCA AAT GTT TTA AAG GTC TTA AAA AAA TTA TTA AAA GTG GGC AAG AAA TGT TGT AAA CAT 1320
 1371 I L L L V E V E R H L G K V G S K C C K H 440

1451 GGT GAA TTA AAA AAT AAT GTC TGT GCA GAA GAC TAT CTA TCC GTG GTC CTG AAC CAG TTA 1380
 1461 F E A K F M F C A E D Y L S V V L N Q L 460

1541 TGT GTC TTS CAT GAT GAT AAA AAG CCA GTA ACT GAC AGA GTC ACA AAA TGC TGC ACA GAG TCC 1440
 1551 C V L L H E K T P V S D R V T K C C T E S 480

Figure 15C

1441 TTG GTG AAC AGG GGA GGA TGC TTT TCA GGT CTG GAA GTC GAT GAA ACA TAC GTT CCC AAA 1500
 481 L V D R R P C F S A L E V D E T Y V P K 500

1501 GAG TTT AAT GCT GAA ACA TGC ACC TTC CAT GCA GAT ATA TGC ACA CTT TCT GAG AAG GAG 1560
 501 E F D A E T F T F H A D I C T L S E K E 520

1561 AGA GAA AAT AAC AAA GAA AAT TTA CTT GAG CTT GTG AAA CAC AAG CCC AAG GCA ACA 1620
 521 R Q I K E V F A L V E L V K H K P K A T 540

1621 AAA GAG GAA CTG AAA GGT GTT ATG GAT GAT TTC GCA GGT TTT GTA GAG AAG TGC TGC AAG 1680
 541 K E Q L K A A V M D E F A A A F V E K C C K 560

1681 GCT GAC GAT AAA GAG AAT TGC TTT GAG GAG GGT AAA CTT GTT GCT GCA AGT CAA 1740
 561 A D D K E T C F A E E G K K L V A A S Q 580

1741 GCT CTC TTA GAG TTA TAA GAT TTA CAT TTA AAA GCA TCT CAG 1782
 581 A A C C L . 585

Figure 15D